Augmentation of HIV Env vaccine efficacy by DC targeting

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Abstract
DESCRIPTION provided by applicant Protection against and control of HIV and SHIV in natural infections and in animal models correlate with the ability of anti Env antibodies to neutralize HIV isolates While sophisticated binding studies using highly mutated and broadly neutralizing antibodies

bnAbs have led to the identification of regions of vulnerability on the Env protein Env vaccine using some of these regions have failed to elicit similarly high affinity bnAbs instead inducing robust antibody responses but with only modest levels of mutations Here we propose a new approach to persistently stimulate B cell clonal lineages so as to generate highly mutated affinity matured neutralizing antibodies and or enhanced non neutralizing FcR mediated functions by harnessing the natural adjuvant properties of a particular subset of CLEC A dendritic cells DCs known to induce very strong humoral immunity In this application we propose to target CLEC A on macaque DCs using anti CLEC A Env fusion proteins produced in plants to achieve antibody mediated delivery of Env immunogens to this DC subset This approach is highly relevant for HIV vaccines since anti Clec A fusion proteins have been shown in mice to efficiently generate T follicular helper cell Tfh responses known to play an important role in the development of HIV SIV specific B cell responses by facilitating somatic mutation and selecting high affinity memory and plasma B cells This macaque study which aims to drive B cell affinity maturation is a collaboration between Dr Bart Haynes who will design the initial prime and boost Env adjuvant vaccine regimens and PlantVax who will produce and provide the final boost with anti CLEC A Env fusion proteins PUBLIC HEALTH RELEVANCE The HIV vaccine trials to date have not been successful in producing the broadly neutralizing antibodies bnAbs that recognize the HIV viral envelope Env protein and that are required for preventing infection In the present study we plan to link the HIV Env protein to an antibody that binds to a receptor on a subset of dendritic cells known to induce very strong antibody responses Using this approach we shall deliver a final boost of this fusion molecule to macaques that have previously been immunized several times with the HIV Env in order to drive their antibody forming B cells to proliferate and produce mutated anti Env antibody similar to the critical bnAbs

* information listed above is at the time of submission.